Electronic Supplementary Material (ESI) for Metallomics.
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Supplementary Information

Gene expression profiling of copper-resistant Caco-2 clones

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Fig. S1. Toxicity profiles of parental and copper resistant Caco-2 clones Or1, Or2, Or3, In1 and In2. Relative cell survival of Caco-2 clones during exposure to increasing concentrations of A: $CuSO_4$, B: Cu proteinate (N>3). X-axis represented in logarithmic scale. Asterisk indicates significant difference from parental Caco-2 (** = P < 0.01)

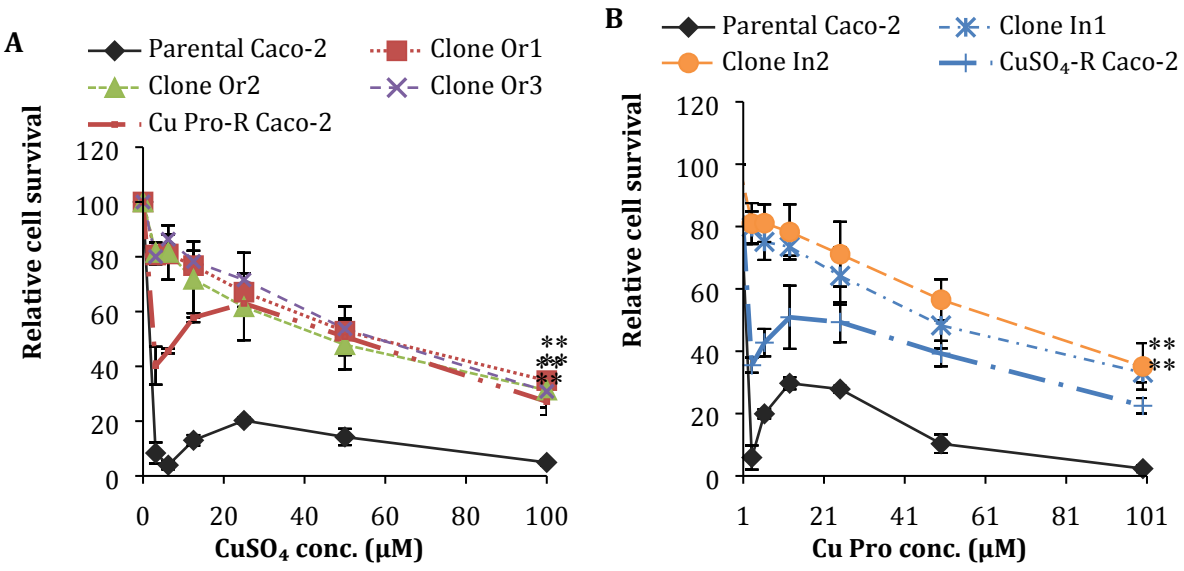

Fig. S2. Relative mRNA expression determined by qRT-PCR for: ANXA13, GPx2, AIFM2, ATP7B and UPK1B in Caco-2 and Cu-resistant clones In1, In2, Or1, Or2 and Or3. Parental Caco-2 exposed to 50 µM $CuSO_4$ and Cu proteinate also shown. β-actin used as endogenous control. Logarithmic scale used for ANXA13 and UPK1B for clarity. Asterisk indicates significant difference from parental population (* = $P < 0.05$). N=3

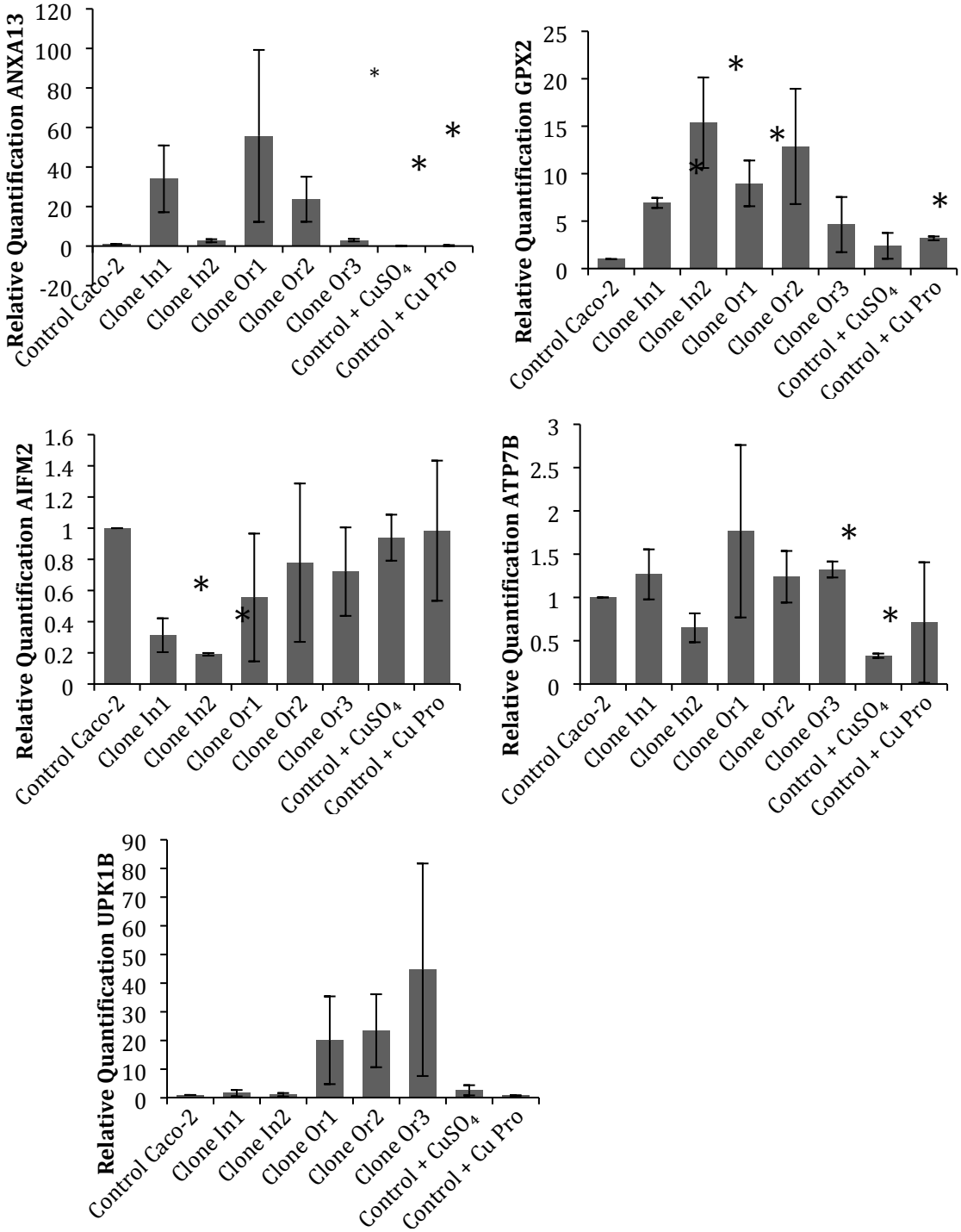

Fig. S3. Gene expression relative fold-change as determined by microarray analysis for: ANXA13, GPx2, AIFM2, ATP7B and UPK1B in Caco-2 and Cu-resistant clones In1, In2, Or1, Or2 and Or3. Only targets detected as differentially expressed in the microarray are shown. False discovery rate adjusted P-values are given above each result determined as significantly different relative to control Caco-2. N=3

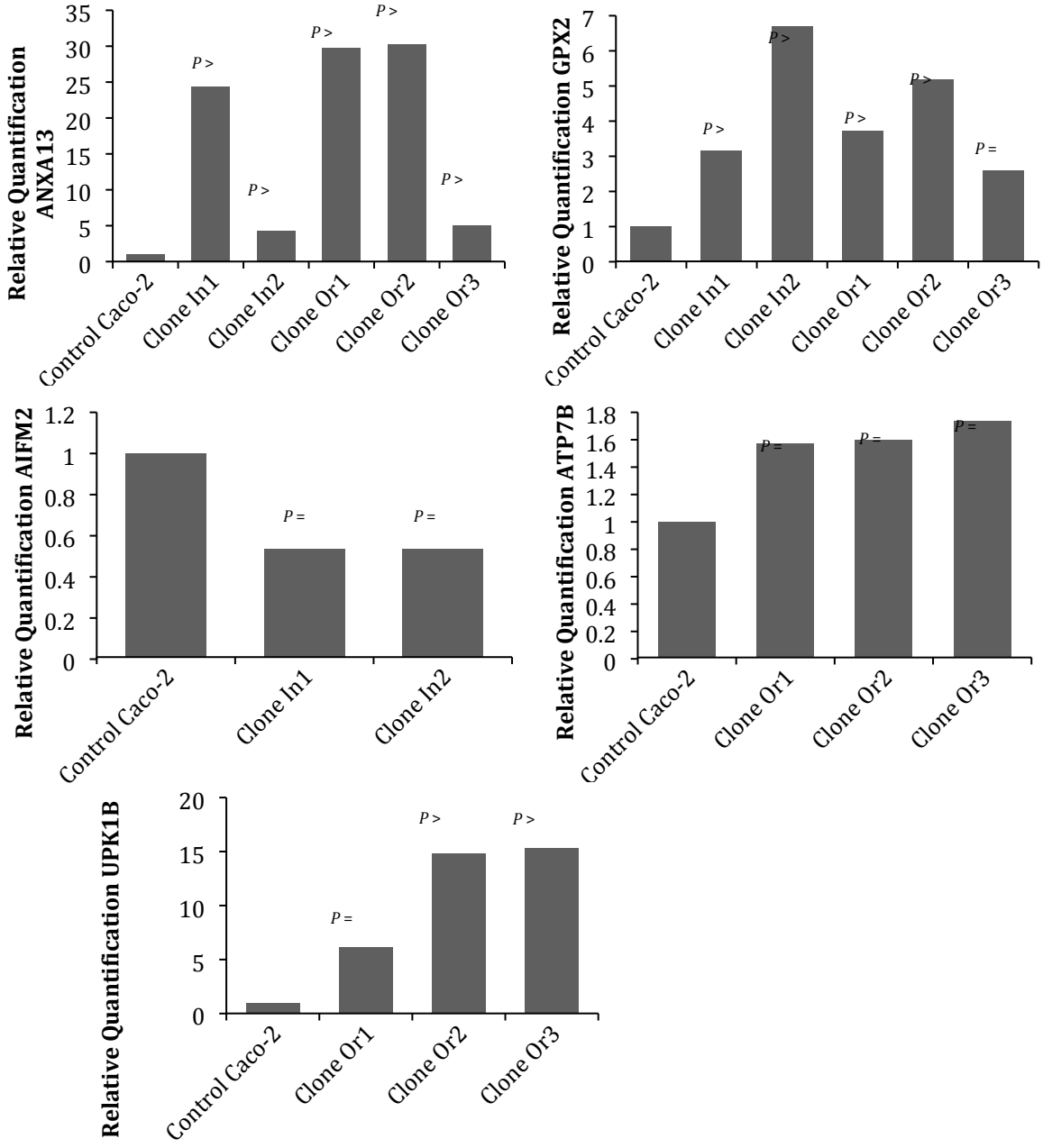

Table S1. List of primers for qRT-PCR, supplied by Invitrogen™ Custom DNA Oligos (Thermo Fischer)

Gene name	Forward	Reverse
ANXA13	5'-GGTTCGCTCAGATACCTCCG-3'	5'-TTCCTATTGCCCTGGCTTGG-3'
ATP7B	5'-GTGGGCAATGACACCACTTT-3'	5'-TGGGTGCCTTTGACATCTGA-3'
GPX2	5'-AGCTCATCATTTGGAGCCCT-3'	5'-TTGATGGTTGGGAAGGTGCG-3'
AIFM2	5'-ATGGTTCGGCTGACCAAGAG-3'	5'-GCCACCACATCATTGGCATC-3'
UROPLAKIN 1B	5'-GGCGTAAATGGTCCATCAGA-3'	5'-AGGCGTGTCGGTTCATTGGA-3'
β-actin	5'-TGGACATCCGCAAAGACCTGTA-3'	5'-TCAGGAGGAGCAATGATCTTGA-3'

Table S2. DAVID UniProt keywords associated with common differentially expressed genes >2 fold in at least 4 of 5 Cu-resistant Caco-2 clones (331 genes input into DAVID version 6.8). Only annotations with P value less than 0.05 shown.

	Gene Count	*P* value
Signal	89	0.000025
Glycoprotein	95	0.00003
Membrane	135	0.00036
Secreted	47	0.00042
Stress response	8	0.00054
Annexin	4	0.0009
Calcium/phospholipid-binding	4	0.0011
Transmembrane helix	101	0.0044
Chloride channel	5	0.0057
Disulfide bond	64	0.015
EGF-like domain	9	0.02
Chloride	5	0.02
SH3 domain	8	0.033
Pyrrolidone carboxylic acid	5	0.043